SYNLETT
Spotlight 209

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Trimethylsilyl Azide ($TMSN_3$): A Versatile Reagent in Organic Synthesis

Compiled by Mohammad Jafarzadeh

M. Jafarzadeh was born in Babol, Iran. He received his bachelor degree in chemistry from the Islamic Azad University, North Tehran Branch in 1998. He continued his studies in organic chemistry at Kurdistan University, Sanandaj, Iran in 2001, where he investigated the application of heteropoly acids in organic synthesis under the guidance of Dr. Kamal Amani for his M.Sc. degree. Currently he is working towards his Ph.D under the supervision of Prof. I. A. Rahman at the Universiti Sains Malaysia. His research interests focus on green chemistry and nanoscience.

School of Chemical Science, Universiti Sains Malaysia, 11800 Minden, Penang Island, Malaysia
E-mail: m_jafarzadeh@chemist.com

Dedicated to Prof. M. M. Khodaei, who is a respected mentor in my life.

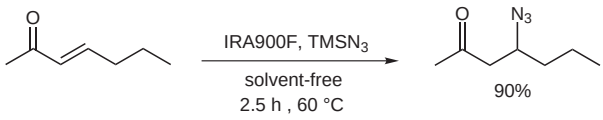
Introduction

In recent times, azides have received much attention in synthetic organic chemistry. The azide moiety is a versatile functional group that serves many purposes in organic synthesis and azides can react very differently under different reaction conditions. In spite of their less-attractive properties (explosiveness, toxicity), a plethora of new applications has been published.[1] Silyl azides are valuable reagents in organic synthesis because they have, unlike sodium azide and hydrogen azide, no immediate explosive properties. However, they hydrolyze in the long term to the volatile, toxic, and explosive hydrogen azide and therefore must be stored in the absence of moisture and acids. Trimethylsilyl azide (Me_3SiN_3; bp 95 ºC), which is also commercially available, can be prepared from trimethylsilyl chloride by reaction with sodium azide in diglyme.[2]

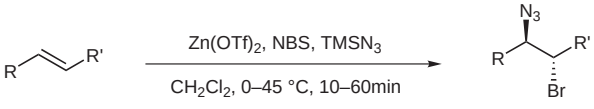
In the last years, there has been growing interest in this compound that has been used as a fruitful reagent for synthesis of triazoles,[3] tetrazoles,[4] glycosyl azides,[5] β-silyl azides,[6] azirines,[7] nitriles,[8] for β-azidation of α,β-unsaturated carbonyl compounds,[9] carboazidation of allenes,[10] azidophenylselenylation of glycals,[11] ring opening of aziridines,[12] oxazolines,[13] and epoxides.[14]

Abstracts

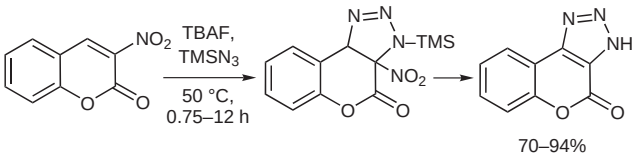
(A) Polystyrene-supported ammonium fluoride (Amberlite IRA900F) is an excellent polymer-supported organocatalyst which has been used for the aza-Michael azidation of α,β-unsaturated ketones with $TMSN_3$ under solvent-free conditions with good to excellent yields. The catalyst was recycled and reused in four more runs without loss of its efficiency and activity.[15]



(B) Regio- and stereoselective bromoazidation of alkenes was carried out using *N*-bromosuccinimide (NBS) and $TMSN_3$ as bromine and azide source with good yields. Zinc triflate [$Zn(OTf)_2$] was an efficient catalyst for the synthesis of *anti*-1,2-bromoazide with high selectivity.[16] Also, bromoazidation of α,β-unsaturated carbonyl compounds has been performed with $Yb(OTf)_3$ as catalyst.[17]

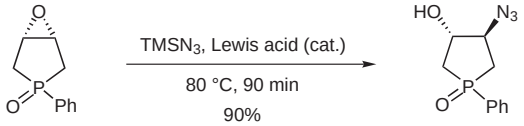


(C) Tetrabutylammonium fluoride (TBAF) has been utilized in the [3+2] cycloaddition of $TMSN_3$ to variously substituted 3-nitrocoumarins[18] and nitroethenes[19] under solvent-free conditions in high yields. This approach is defined as an environmentally benign protocol for accessing a new class of fused triazoles.

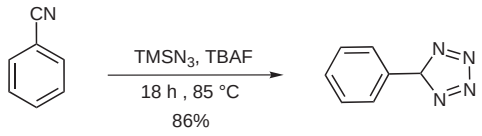


SYNLETT 2007, No. 13, pp 2144–2145
Advanced online publication: 12.07.2007
DOI: 10.1055/s-2007-984895; Art ID: V21207ST

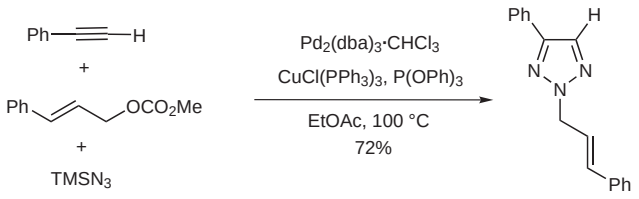
(D) Asymmetric ring-opening of the epoxides by $TMSN_3$ in the presence of a salen–Al complex as chiral Lewis acid catalyst is demonstrated. The results revealed high enantioselectivity for the synthesis of *trans*-3-hydroxy-4-azidooxides from achiral epoxyphenylphospholane oxide.[20]



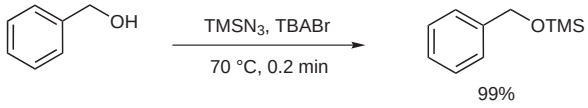
(E) Vaccaro and co-workers described a [3+2] cycloaddition of organic nitriles with $TMSN_3$ under mild conditions affording 80–97% yields. TBAF was an efficient catalyst in the solvent-free synthesis of 5-substituted 1*H*-tetrazoles.[21] Also dibutyltin oxide [$Bu_2Sn(O)$] can be used for this reaction.[22]



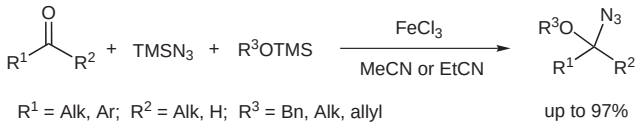
(F) Yamamoto and co-workers reported a one-pot procedure for the regioselective synthesis of allyltriazides via three-component coupling reaction between non-activated terminal alkynes[23] or silylacetylenes,[24] allyl carbonate and $TMSN_3$. The palladium/copper bimetallic catalyst was successfully applied for the formation of 1-allyl-1,2,3-triazoles.



(G) Trimethylsilylation of a wide variety of alcohols, phenols and diols were performed under neat conditions with $TMSN_3$. Tetrabutylammonium bromide (TBABr) was an efficient catalyst that activated the silicon atom towards nucleophilic attack.[25]



(H) The synthesis of α-alkoxy azides was carried out in a one-pot reaction of the aromatic and aliphatic aldehydes or ketones with alkoxytrimethylsilane and $TMSN_3$. This procedure was promoted using iron(III) chloride as an inexpensive and commercially available catalyst under mild conditions with excellent yield.[26]



References

(1) Cenini, S.; Gallo, E.; Caselli, A.; Ragaini, F.; Fantauzi, S.; Piangiolino, C. *Coord. Chem. Rev.* **2006**, *250*, 1234.
(2) Bräse, S.; Gil, C.; Knepper, K.; Zimmermann, V. *Angew. Chem. Int. Ed.* **2005**, *44*, 5188.
(3) (a) Yanai, H.; Taguchi, T. *Tetrahedron Lett.* **2005**, *46*, 8639. (b) Kamijo, S.; Jin, T.; Huo, Z.; Yamamoto, Y. *Tetrahedron Lett.* **2002**, *43*, 9707.
(4) (a) Jin, T.; Kamijo, S.; Yamamoto, Y. *Tetrahedron Lett.* **2004**, *45*, 9435. (b) Cristau, H.-J.; Marat, X.; Vors, J.-P.; Pirat, J.-L. *Tetrahedron Lett.* **2003**, *44*, 3179.
(5) (a) Reddy, B. G.; Madhusudanan, K. P.; Vankar, Y. D. *J. Org. Chem.* **2004**, *69*, 2630. (b) Yadav, J. S.; Reddy, B. V. S.; Chand, P. K. *Tetrahedron Lett.* **2001**, *42*, 4057.
(6) Chabaud, L.; Landais, Y. *Tetrahedron Lett.* **2003**, *44*, 6995.
(7) Pinho e Melo, T. M. V. D.; Lopes, C. S. J.; Cardoso, A. L.; Rocha Gonsalves, A. M. d'A. *Tetrahedron* **2001**, *57*, 6203.
(8) Sandberg, M.; Sydnes, L. K. *Tetrahedron Lett.* **1998**, *39*, 6361.
(9) Adamo, L.; Benedetti, F.; Berti, F.; Campaner, P. *Org. Lett.* **2006**, *8*, 51.
(10) Chang, H. M.; Cheng, C. H. *J. Chem. Soc., Perkin Trans 1* **2000**, 3799.
(11) Mironov, Y. V.; Sherman, A. A.; Nifantiev, N. E. *Tetrahedron Lett.* **2004**, *45*, 9107.
(12) (a) Hu, X. E. *Tetrahedron* **2004**, *60*, 2701. (b) Reddy, M. A.; Reddy, L. R.; Bhanumathi, N.; Rao, K. R. *Chem. Lett.* **2001**, 246. (c) Wu, J.; Hou, X. L.; Dai, L. X. *J. Org. Chem.* **2000**, *65*, 1344. (d) Chandrasekhar, M.; Sekar, G.; Singh, V. K. *Tetrahedron Lett.* **2000**, *41*, 10079.
(13) Lee, S. H.; Yoon, J.; Chung, S. H.; Lee, Y. S. *Tetrahedron* **2001**, *57*, 2139.
(14) (a) Konno, H.; Toshiro, E.; Hinoda, N. *Synthesis* **2003**, 2161. (b) Schneider, C. *Synlett* **2000**, 1840.
(15) Castrica, L.; Fringuelli, F.; Gregoli, L.; Pizzo, F.; Vaccaro, L. *J. Org. Chem.* **2006**, *71*, 9536.
(16) Hajra, S.; Sinha, D.; Bhowmick, M. *Tetrahedron Lett.* **2006**, *47*, 7017.
(17) Hajra, S.; Bhowmick, M.; Sinha, D. *J. Org. Chem.* **2006**, *71*, 9237.
(18) D'Ambrosio, G.; Fringuelli, F.; Pizzo, F.; Vaccaro, L. *Green Chem.* **2005**, *7*, 874.
(19) Amantini, D.; Fringuelli, F.; Piermatti, O.; Pizzo, F.; Zunino, E.; Vaccaro, L. *J. Org. Chem.* **2005**, *70*, 6526.
(20) Pakulski, Z.; Pietrusiewicz, K. M. *Tetrahedron: Asymmetry* **2004**, *15*, 41.
(21) Amantini, D.; Beleggia, R.; Fringuelli, F.; Pizzo, F.; Vaccaro, L. *J. Org. Chem.* **2004**, *69*, 2896.
(22) Schulz, M. J.; Coats, S. J.; Hlasta, D. J. *Org. Lett.* **2004**, *6*, 3265.
(23) Kamijo, S.; Jin, T.; Huo, Z.; Yamamoto, Y. *J. Org. Chem.* **2004**, *69*, 2386.
(24) Kamijo, S.; Jin, T.; Yamamoto, Y. *Tetrahedron Lett.* **2004**, *45*, 689.
(25) Amantini, D.; Fringuelli, F.; Pizzo, F.; Vaccaro, L. *J. Org. Chem.* **2001**, *66*, 6734.
(26) Omura, M.; Iwanami, K.; Oriyama, T. *Chem. Lett.* **2007**, 532.